Punjab University
Journal of Mathematics (ISSN 1016-2526)
Vol. 51(2)(2019) pp. 105-121

Modeling and Control of Zoonotic Cutaneous Leishmaniasis

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Received: 19 September, 2017 / Accepted: 29 May, 2018 / Published online: 17 December, 2018

Abstract. This work focuses on mathematical modeling and control of Zoonotic Cutaneous Leishmania. The model includes human, reservoir and vector populations. Using next generation matrix threshold condition, R_0, for initial rate of transmission of the infection is obtained. After biological interpretation of R_0, its sensitivity analysis is conducted. On the basis of sensitivity analysis some strategies are proposed for elimination of the disease. The strategies quantify the relation between the elimination periods and the interventions opted. For validation of the results we use Runge-Kutta method in our numerical simulations.

AMS Subject Classification Code: 92Bxx
Key Words: Leishmaniasis, Basic reproduction number, Mathematical model, Sensitivity.

1. INTRODUCTION

Leishmaniasis is a group of infectious diseases. The parasite of the genus Leishmania is the causative agent of the disease. The parasite is carried from the source to the sank

by sand fly (phlebotomine). The fly is about $2-3$ mm long. The four main clinical manifestation of the disease are [1, 2].

- Muco-Cutaneous Leishmaniasis
- Cutaneous Leishmaniasis
- Post -Kala-Azar Dermal Leishmaniasis (PKDL)
- Visceral Leishmaniasis or Kala-Azar.

The global prevalence of leishmaniasis among human population is estimated to be about 10 millions. The annual registering number of new clinical cases varies from 1.5 to 2.5 millions [3]. The most common kind of Leishmaniasis found in the world, is Cutaneous Leishmaniasis. Its incubation period generally varies between two weeks to eight weeks, however the duration may exceeds the mentioned period [4]. L-major is the causative agent of human Cutaneous Leishmaniasis. After recovery from the Cutaneous strain of Leishmania the recovered individual develops long term immunity. The immunity acquired due to vaccination is short term [5, 6].
After contact with infectious human or reservoir, the sand fly catches infection. The latency period of sand fly varies between three to seven days [7].
Different researchers have worked on mathematical modeling of different issues like air pollution, Human brain memory and Leishmaniasis etc. The recent work includes [8, 9, 10, 11, 12, 13]. These studies have focus different dynamics of the target issues.
Zamir et al. [14], proposed a mathematical of Anthroponotic Cutaneous strain of Leishmaniasis ACL. They in their study discuss different dynamics of (ACL). The authors particularly discuss, different stages of the infectious state and their role in disease transmission in human class. Finally the authors proposed some control strategies for elimination of the disease.
We in this work, design control strategies for eradication of Zoonotic Cutaneous Leishmaniasis. For this we propose mathematical model and apply next generation matrix method to find the reproduction number R_0 of the model. We conduct sensitivity analysis of the parameters involved in R_0. On the basis of sensitivity indices of the parameters, we propose control strategies.

2. Mathematical analysis of the model

In this section we discuss the formulation of mathematical model and invariant region.

Model formulation:

Zoonotic Cutaneous Leishmaniasis mainly effects the three populations; Human, sand fly and reservoir. We sub-divided each population in different sub-classes. Human population is divided in four sub-classes; the susceptible class S_h the latent class E_h the infectious class I_h and the recovered class R_h .
The total human population is

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t).$$

The sub-classes of the vector population are the susceptible sand flies $S_v(t)$ the exposed sand flies $E_v(t)$ and the infectious sand flies $I_v(t)$.
The total vector population is

$$N_v(t) = S_v(t) + E_v(t) + I_v(t).$$

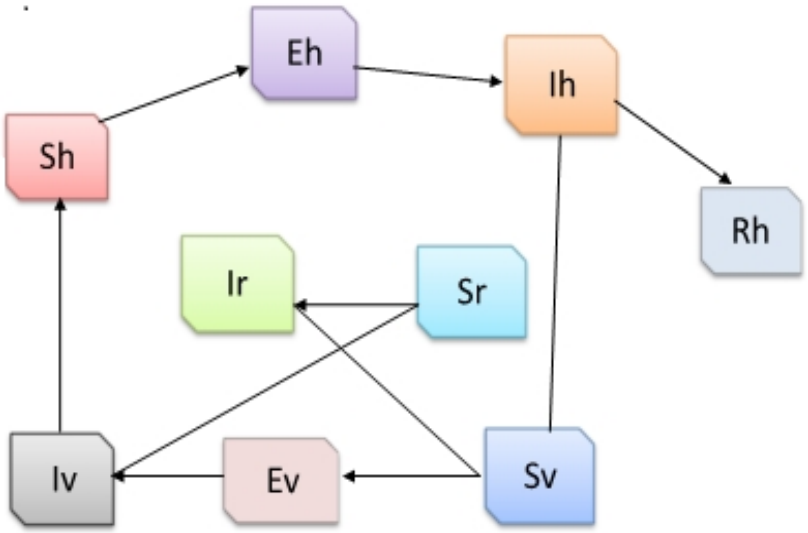

FIGURE 1

The reservoir class is sub-divided into two sub-classes, The susceptible reservoirs $S_r(t)$ and the infectious reservoirs $I_r(t)$. Total reservoir population is

$$N_r(t) = S_r(t) + I_r(t).$$

The constant per capita human recruitment rate is Γh. As result of the interaction between susceptible human and infected sand fly, the human catches infection at the rate $\frac{ab_1 I_v}{N_h+N_r}$ and moves to the exposed class, here $'a'$ shows the biting rate of sand fly and b_1 is the transmission probability of Cutaneous Leishmaniasis from sand fly to human [15]. Some of the exposed individuals recover naturally at the rate θ and the rest of exposed humans get infectious at the rate k_1 . The fraction of the infected humans are naturally recovered at the rate β and some recover due to treatment at the rate γ .
Γr is the recruitment rate of the reservoir. When an infected sand fly contact a susceptible reservoir to collect blood meal, the reservoir catches infection at the rate $\frac{abI_v}{N_h+N_r}$ and move to the infectious class, here a shows the biting rate of sand fly and b is the transmission probability of Cutaneous Leishmaniasis from sand fly to reservoir.
$\Gamma v$is the recruitment rate of sand flies . Sand flies can catch disease as a result of contact with infected humans or infected reservoirs. Sand flies are infected after contact with infected humans and reservoirs at the rate $\frac{a(c_1 I_h+cI_r)}{N_h+N_r}$, here c_1 and c are the transmission probabilities of Cutaneous Leishmaniasis from human to sand fly and from reservoir to sand fly respectively. When incubation period is completed, the sand flies get infectious at the rate k_2.
Figure (1) presents the flowchart of disease transmission among vectors, humans and reservoirs; Disease transmission in different populations is shown by the coupled non-linear

system of differential equation (2. 1).

$$\begin{cases} \dot{S_h} = \Gamma_h - \frac{ab_1 I_v S_h}{N_h+N_r} - \mu_h S_h \\ \dot{E_h} = \frac{ab_1 I_v S_h}{N_h+N_r} - (k_1+\theta+\mu_h)E_h \\ \dot{I_h} = k_1 E_h - (\gamma+\beta+\mu_h)I_h \\ \dot{R_h} = \theta E_h + (\gamma+\beta)I_h - \mu_h R_h \\ \dot{S_r} = \Gamma_r - \frac{abI_v S_r}{N_h+N_r} - \mu_r S_r \\ \dot{I_r} = \frac{abI_v S_r}{N_h+N_r} - (\mu_r+\mu_2)I_r \\ \dot{S_v} = \Gamma_v - \frac{a(c_1 I_h+cI_r)S_v}{N_h+N_r} - \mu_v S_v \\ \dot{E_v} = \frac{a(c_1 I_h+cI_r)S_v}{N_h+N_r} - (\mu_v+k_2)E_v \\ \dot{I_v} = k_2 E_v - \mu_v I_v. \end{cases} \quad (2.\ 1)$$

The transmission rate of cutaneous strain from reservoir to sand fly [16], CL progression rate in reservoir [17], the incubation period of CL in human and sand fly [18, 7], natural mortality rates of human, reservoir and sand fly [19, 20, 21], sand fly biting rate [22], recruitment rates of sand flies, humans and reservoirs [6, 23, 25], natural recovery rate of CL in human [26], and the transmission probability of CL from human to sand fly [25, 27] are shown in table (1).

Invariant Region:

All the parameters used in the model are nonnegative. Since the model is concerned with living population, therefore the state variables used in the proposed model are taken nonnegative at t=0. The following differential equations show the disease dynamics in all the three populations.

$$\dot{N_h} = \Gamma_h - \mu_h N_h \quad (2.\ 2)$$

$$\dot{N_r} = \Gamma_r - \mu_r N_r - \mu_2 I_r \quad (2.\ 3)$$

$$\dot{N_v} = \Gamma_v - \mu_v N_v. \quad (2.\ 4)$$

The non-negative equilibriums of above equations are (if there is no disease)

$$N_h = \frac{\Gamma_h}{\mu_h},\ N_r = \frac{\Gamma_r}{\mu_r},\ N_v = \frac{\Gamma_v}{\mu_v}.$$

Consider the biological feasible region Ψ given by

$$\Psi = \left[(S_h, E_h, I_h, R_h, S_r, I_r, S_v, E_v, I_v) \in R_+^9\ , N_h \leq \frac{\Gamma_h}{\mu_h}; N_r \leq \frac{\Gamma_r}{\mu_r}; N_v \leq \frac{\Gamma_v}{\mu_v} \right].$$

From $equation\ (2)$, using Standard comparison theorem, we have

$$N_h = N_h(0)e^{-\mu_h(t)} + \frac{\Gamma_h}{\mu_h}\left(1 - e^{-\mu_h(t)}\right).$$

So

$$N_h \to \frac{\Gamma_h}{\mu_h}\ as\ t \to \infty.$$

similarly

$$\left[N_r \to \frac{\Gamma_r}{\mu_r}\ and\ N_v \to \frac{\Gamma_v}{\mu_v} \right]\ as\ t \to \infty.$$

TABLE 1. values of the parameters

Notation	Parameter definition	Value	Resource
c	CL transmission rate from reservoir to sand fly	$0.22day^{-1}$	[16]
b	CL Progression rate in reservoir	$0.0714day^{-1}$	[17]
Γ_v	Recruitment rate of sandfly	$0.299day^{-1}$	[6]
k_1	$1/k_1$ is incubation period of cl in human	$0.0157871day^{-1}$	[18]
k_2	$1/k_2$ is incubation period of cl in sand fly	$0.2day^{-1}$	[7]
μ_2	Rate of CL induced death rate in dogs	$0.0008day^{-1}$	Assumed
μ_h	Natural mortality rate of human	$0.00004day^{-1}$	[19]
μ_r	Natural mortality rate of Reservoirs	$0.000274day^{-1}$	[20]
μ_v	Natural mortality rate of Sandflies	$0.189day^{-1}$	[21]
a	Sandflies biting rate	$0.2856day^{-1}$	[22]
Γ_h	Recruitment rate of human	$0.0015875day^{-1}$	[23]
Γ_r	Recruitment rate of reservoir	$0.073day^{-1}$	[25]
γ	CL Recovery rate from infectious class (treatment)	$0.0306day^{-1}$	[26]
β	CL Natural rate of recovery	$0.0056day^{-1}$	[26]
c_1	CL transmission rate in sand fly (from human)	0.28	[25, 27]
b_1	CL transmission rate in human (from sand fly)	$0.1day^{-1}$	[25, 27]
θ	CL Recovery rate from exposed class	$0.0139day^{-1}$	Assumed

Thus N_h, N_v and N_r are forward bounded. So Ψ is positively invariant domain and the frame is mathematically and epidemiologically well posed [28].

3. INITIAL RATE OF DISEASE TRANSMISSION

In this section we discuss threshold condition for initial rate of disease transmission, biological interpretation of the reproduction number and sensitivity analysis of different parameters used in the model.

3.1. **Reproduction Number:** When an infectious individual enters a susceptible population, the infection spread in the population. The number of secondary infections occurring

in population is called reproduction number R_0. Initial rate of disease transmission, is infact, the reproduction number of system (1) [18].
Next generation matrix method is used to find for the system (1) [23, 24].
To find R_0 , we use the formula

$$R_0 = \rho(-FV^{-1}),$$

Where ρ is spectral radius.
Here

$$f = \begin{pmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \\ f_5 \end{pmatrix} = \begin{pmatrix} \frac{ab_1 I_v S_h}{N_h+N_r} \\ 0 \\ \frac{abI_v S_r}{N_h+N_r} \\ \frac{a(c_1 I_h + cI_r)S_v}{N_h+N_r} \\ 0 \end{pmatrix}$$

The entries of the column in matrix f denotes the individuals who caught infection.

$$F = \begin{pmatrix} \frac{\partial(f_1)}{\partial(E_h)} & \frac{\partial(f_1)}{\partial(I_h)} & \frac{\partial(f_1)}{\partial(I_r)} & \frac{\partial(f_1)}{\partial(E_v)} & \frac{\partial(f_1)}{\partial(I_v)} \\ \frac{\partial(f_2)}{\partial(E_h)} & \frac{\partial(f_2)}{\partial(I_h)} & \frac{\partial(f_2)}{\partial(I_r)} & \frac{\partial(f_2)}{\partial(E_v)} & \frac{\partial(f_2)}{\partial(I_v)} \\ \frac{\partial(f_3)}{\partial(E_h)} & \frac{\partial(f_3)}{\partial(I_h)} & \frac{\partial(f_3)}{\partial(I_r)} & \frac{\partial(f_3)}{\partial(E_v)} & \frac{\partial(f_3)}{\partial(I_v)} \\ \frac{\partial(f_4)}{\partial(E_h)} & \frac{\partial(f_4)}{\partial(I_h)} & \frac{\partial(f_4)}{\partial(I_r)} & \frac{\partial(f_4)}{\partial(E_v)} & \frac{\partial(f_4)}{\partial(I_v)} \\ \frac{\partial(f_5)}{\partial(E_h)} & \frac{\partial(f_5)}{\partial(I_h)} & \frac{\partial(f_5)}{\partial(I_r)} & \frac{\partial(f_5)}{\partial(E_v)} & \frac{\partial(f_5)}{\partial(I_v)} \end{pmatrix}$$

$$= \begin{pmatrix} 0 & 0 & 0 & 0 & \frac{ab_1 S_h}{N_h+N_r} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{abS_r}{N_h+N_r} \\ 0 & \frac{ac_1 S_v}{N_h+N_r} & \frac{acS_v}{N_h+N_r} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

For simplicity we write F as

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & n_1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & n_2 \\ 0 & n_3 & n_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}_{(DFE)}$$

$'DFE'$ stands for disease free equilibrium state of the population.

And

$$v = \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{pmatrix} = \begin{pmatrix} -(k_1 + \theta + \mu_h)E_h \\ k_1 E_h - (\gamma + \beta + \mu_h)I_h \\ -(\mu_r + \mu_2)I_r \\ -(\mu_v + k_2)E_v \\ k_2 E_v - \mu_v I_v \end{pmatrix}$$

The column of matrix v denotes the individuals that enter the infected class or leave the infected class, excluding those coming from susceptible class.

$$V = \begin{pmatrix} \frac{\partial(v_1)}{\partial(E_h)} & \frac{\partial(v_1)}{\partial(I_h)} & \frac{\partial(v_1)}{\partial(I_r)} & \frac{\partial(v_1)}{\partial(E_v)} & \frac{\partial(v_1)}{\partial(I_v)} \\ \frac{\partial(v_2)}{\partial(E_h)} & \frac{\partial(v_2)}{\partial(I_h)} & \frac{\partial(v_2)}{\partial(I_r)} & \frac{\partial(v_2)}{\partial(E_v)} & \frac{\partial(v_2)}{\partial(I_v)} \\ \frac{\partial(v_3)}{\partial(E_h)} & \frac{\partial(v_3)}{\partial(I_h)} & \frac{\partial(v_3)}{\partial(I_r)} & \frac{\partial(v_3)}{\partial(E_v)} & \frac{\partial(v_3)}{\partial(I_v)} \\ \frac{\partial(v_4)}{\partial(E_h)} & \frac{\partial(v_4)}{\partial(I_h)} & \frac{\partial(v_4)}{\partial(I_r)} & \frac{\partial(v_4)}{\partial(E_v)} & \frac{\partial(v_4)}{\partial(I_v)} \\ \frac{\partial(v_5)}{\partial(E_h)} & \frac{\partial(v_5)}{\partial(I_h)} & \frac{\partial(v_5)}{\partial(I_r)} & \frac{\partial(v_5)}{\partial(E_v)} & \frac{\partial(v_5)}{\partial(I_v)} \end{pmatrix}$$

$$V = \begin{pmatrix} -(k + \theta + \mu_h) & 0 & 0 & 0 & 0 \\ k_1 & -(\gamma + \beta + \mu_h) & 0 & 0 & 0 \\ 0 & 0 & -(\mu_r + \mu_2) & 0 & 0 \\ 0 & 0 & 0 & -(\mu_v + k_2) & 0 \\ 0 & 0 & 0 & k_2 & -(\mu_v) \end{pmatrix}_{(DFE)}$$

For simplicity we write V as

$$V = \begin{pmatrix} -a_1 & 0 & 0 & 0 & 0 \\ k_1 & -a_2 & 0 & 0 & 0 \\ 0 & 0 & -a_3 & 0 & 0 \\ 0 & 0 & 0 & -a_4 & 0 \\ 0 & 0 & 0 & k_2 & -a_5 \end{pmatrix}_{(DFE)}$$

The dominant Eigenvalue of $(-FV^{-1})$ is

$$\left[\frac{k_2 n_2 n_4}{a_3 a_4 a_5} + \frac{k_1 k_2 n_1 n_3}{a_1 a_2 a_4 a_5}\right]^{\frac{1}{2}}$$

So

$$R_0 = \left[\frac{k_2 n_2 n_4}{a_3 a_4 a_5} + \frac{k_1 k_2 n_1 n_3}{a_1 a_2 a_4 a_5}\right]^{\frac{1}{2}}$$

Here

$$n_1 = ab_1\frac{\Gamma_h\mu_r}{\mu_r\Gamma_h+\mu_h\Gamma_r}\ n_2 = ab\frac{\Gamma_r\mu_h}{\mu_r\Gamma_h+\mu_h\Gamma_r}$$

$$n_3 = ac_1\frac{\mu_r\mu_h\Gamma_v}{\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r)}\ n_4 = ac\frac{\mu_r\mu_h\Gamma_v}{\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r)}$$

$$a_1 = k_1+\theta+\mu_h,\ a_2 = \gamma+\beta+\mu_h$$
$$a_3 = \mu_r+\mu_2,\ a_4 = \mu_v+k_2,\ a_5 = \mu_v$$

Let

$$R_0 = \left[R_1+R_2\right]^{\frac{1}{2}}.$$

Then

$$R_1 = \frac{k_2a^2bc\mu_h^2\mu_r\Gamma_r\Gamma_v}{(\mu_r+\mu_2)(\mu_v+k_2)(\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r))^2},$$
$$R_2 = \frac{k_1k_2a^2b_1c_1\mu_h\mu_r^2\Gamma_h\Gamma_v}{(k_1+\theta+\mu_h)(\gamma+\beta+\mu_h)(\mu_v+k_2)(\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r))^2}$$

Thus
$R_0 = \sqrt{\frac{k_2a^2bc\mu_h^2\mu_r\Gamma_r\Gamma_v}{(\mu_r+\mu_2)(\mu_v+k_2)(\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r))^2}+\frac{k_1k_2a^2b_1c_1\mu_h\mu_r^2\Gamma_h\Gamma_v}{(k_1+\theta+\mu_h)(\gamma+\beta+\mu_h)(\mu_v+k_2)(\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r))^2}}.$

3.2. **Biological interpretation of Reproduction Number:** R_0 has got two terms R_1 and R_2. We investigate the Biological interpretation of both R_1 and R_2. Consider R_2

$$R_2 = \frac{k_1k_2a^2b_1c_1\mu_h\mu_r^2\Gamma_h\Gamma_v}{(k_1+\theta+\mu_h)(\gamma+\beta+\mu_h)(\mu_v+k_2)(\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r))^2}$$

Sand fly biting rate is denoted by a and transmission probability of Cutaneous strain from human to sand fly is denoted by b_1.c_1 denotes the transmission probability of disease from human to sand fly. If the sand fly is infected with Cutaneous strain and the human is susceptible. The contact of the two parties would cause the transmission of infection to the human. The term ab_1 of R_2 denotes the said infection. In otherwise case the disease will be transmitted to sand fly as indicated by the term ac_1 of R_2. Therefore R_2 represents the disease transmission between sand fly and human.
Next consider the term R_1 of R_0.

$$R_1 = \frac{k_2a^2bc\mu_h^2\mu_r\Gamma_r\Gamma_v}{(\mu_r+\mu_2)(\mu_v+k_2)(\mu_v(\mu_r\Gamma_h+\mu_h\Gamma_r))^2}.$$

Here b indicates the transmission of infection from sand fly to reservoir. The contact of susceptible reservoir and infected sand fly results in the transmission of disease from sand fly to reservoir. The transmission is indicated by term ab of R_1. In otherwise situation the disease will be transmitted from reservoir to sand fly. In this case the term ac denotes transmission of disease from reservoir to sand fly.
The reason of emphasizing the terms ac_1 , ab_1, ab and ac is that here the direction of

TABLE 2. Sensitivity indices of parameters

Parameter	parameter value	sensitivity index
a	0.2856	$+1$
β	0.0056	-0.000032155
Γ_v	0.299	$+0.5$
Γ_h	0.0015875	-0.1276
Γ_r	0.073	-0.3724
θ	0.0139	-0.000097298
γ	0.0306	-0.0018
b	0.0714	$+0.4979$
b_1	0.1	$+0.0021$
c	0.22	$+0.4979$
c_1	0.28	$+0.0021$
k_1	0.0157871	$+0.000097578$
k_2	0.2	$+0.2429$
μ_v	0.189	-1.2429
μ_h	0.00004	$+0.1276$
μ_r	0.000274	$+0.2454$
μ_2	0.0008	-0.3709

transmission of disease is important. The rest of parameters (terms) used in R_0, only indicate the magnitude of R_0.

3.3. **Sensitivity analysis of R_0:** The change in some parameters cause change in linked variables of the model. This relative change is called the sensitivity of parameter. If the given function x is differentiable with respect to some parameter z, the sensitivity of x for z is then define as [29].

$$\Upsilon_z^x = \frac{\partial x}{\partial z}\frac{z}{x}.$$

In table (2) we show the sensitivity of different parameters of the model.

4. FORMULATION OF CONTROL STRATEGIES

In this section we discuss control strategies of the disease. We use R-K-4 method for numerical simulations to validate the theoretical result.

4.1. **Control Strategies:** The parameters involved in R_0 have got different sensitivity indices as shown in table (3). To control the disease transmission we need to address the parameters with high indices. The index of a parameter measures the change in reproduction number, occurring due to a change in that particular parameter. On the basis of parameter's indices we design strategies for control of the disease.
The biting rate of sand fly has got sensitivity index of 1 . This means that decrease of 10% in biting rate of sand fly causes a decrease of 10% in the initial transmission rate R_0. Reservoir mortality rate μ_r has got sensitivity index 0.2443. So increase of 10% in mortality rate of reservoir causes increase of 2% in R_0. The reason is that increase in mortality of dogs, converges the sand fly biting pressure towards human class. This causes increase in infection over there.
We address some key parameters. These key parameters are linked with the rest of parameters involved in disease transmission. For example if we address the parameter $'a'$; the biting rate of sand flies. This intervention would directly affect the contact rate of sand fly and hence the oogenesis of female sand flies. This causes decrease in birth rate of sand flies. Also the control of contact between human and sand flies, reduces the transmission rate of disease between these populations.
We address the following parameters,

- b; the progression rate of Cutaneous Leishmaniasis.
- a; sand fly biting rate.
- c; progression rate of Cutaneous Leishmaniasis in sand fly from reservoir.
- c_1; progression rate of Cutaneous Leishmaniasis in sand fly from human.
- μ_2; dogs culling rate.
- μ_v; sand fly's natural death rate.
- Γ_v; sand fly natural birth rate.

Assigning different values to the above parameters, we propose the following four control strategies as shown in table (3).

4.2. **Numerical Simulation:** We use R-K-4 method for numerical simulation using matlab. The initial susceptible population of human reservoir and sand fly is taken as $S_h = 1000$,$S_r = 100$and $S_v = 10000$.

Summary of infection control from the figures is presented in the table (4). The term I_hT_s means the time spent in eliminating the human infection I_h , similarly I_rT_s and I_vT_s.

5. Conclusion

In this wok, we propose mathematical model of Zoonotic Cutaneous Leishmaniasis. We investigate the initial transmission rate R_0 and discuss its biological sense. We then

TABLE 3. Control strategies

$Strategies$	a	b	c	c_1	μ_2	μ_v	Γ_v
$Strategy\ 1$	0.2856	0.0714	0.22	0.28	0.0008	0.189	0.299
$Strategy\ 2$	0.0356	0.0214	0.20	0.20	0.0009	0.195	0.229
$Strategy\ 3$	0.1356	0.0214	0.22	0.22	0.0004	0.197	0.219
$Strategy\ 4$	0.0456	0.0314	0.22	0.20	0.008	0.211	0.199

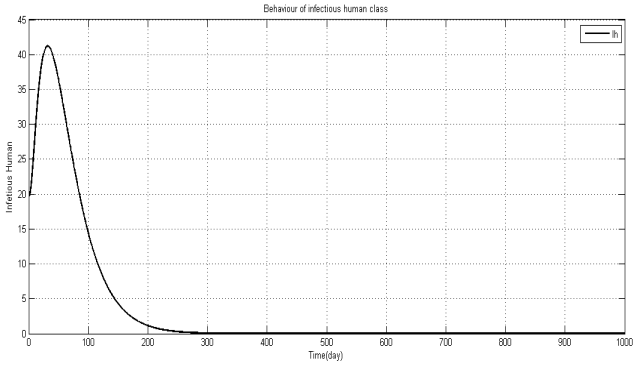

FIGURE 2. Strategy 1, infected human population

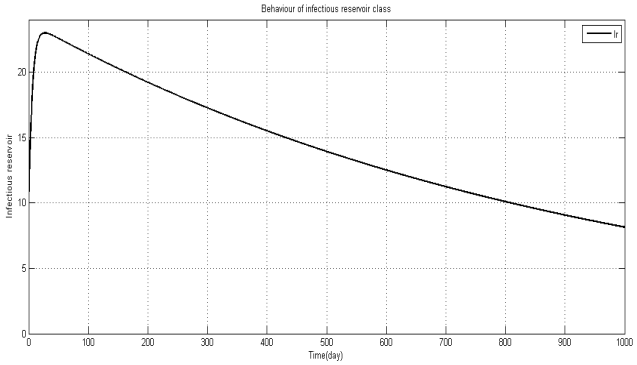

FIGURE 3. Strategy 1, infected reservoir population

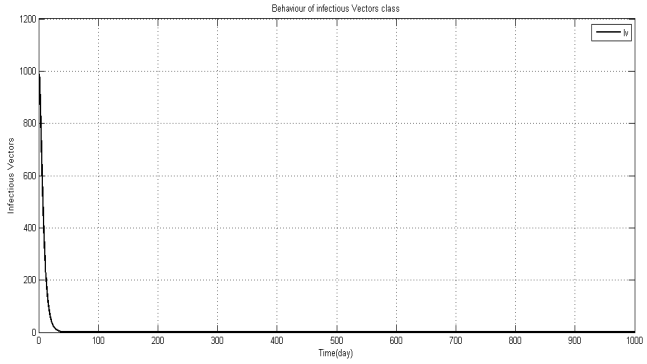

FIGURE 4. Strategy 1, infected vector population

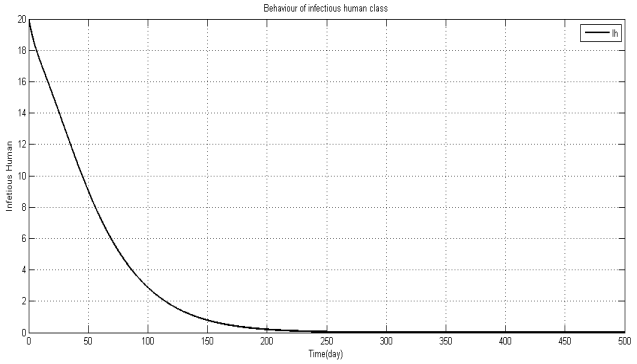

FIGURE 5. Strategy 2, infected human population

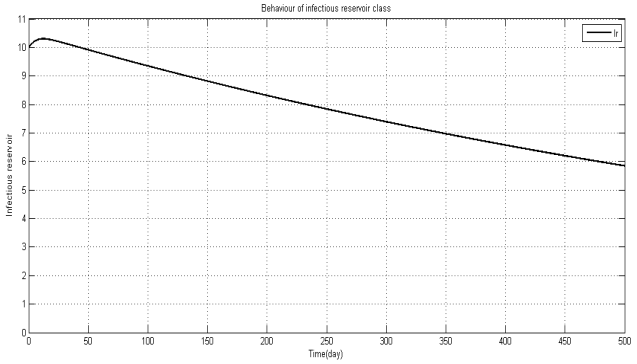

FIGURE 6. Strategy 2, infected reservoir population

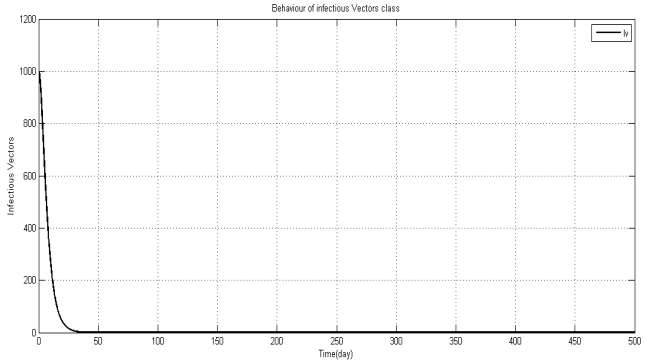

FIGURE 7. Strategy 2, infected vector population

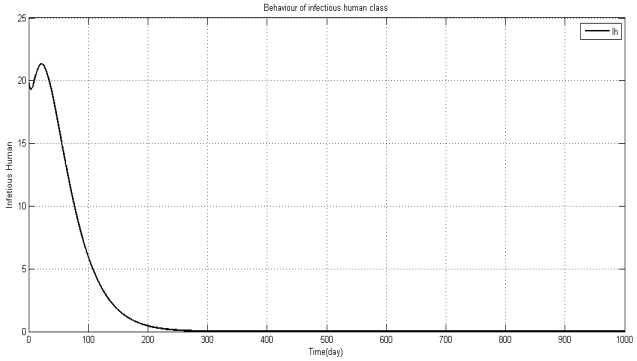

FIGURE 8. Strategy 3, infected human population

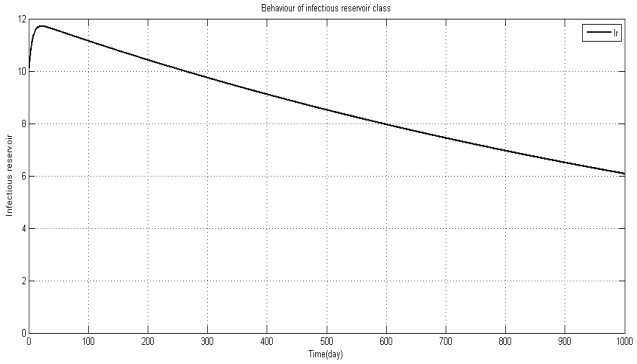

FIGURE 9. Strategy 3, infected reservoir population

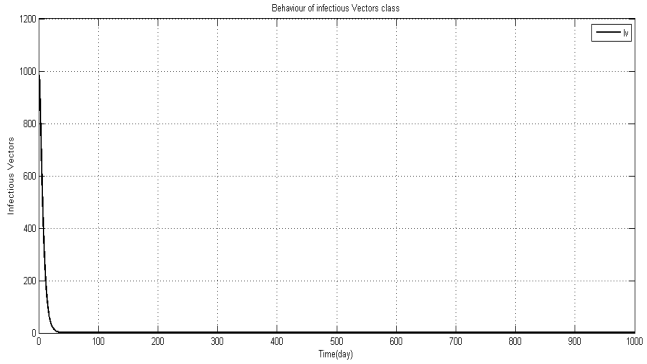

FIGURE 10. Strategy 3, infected vector population

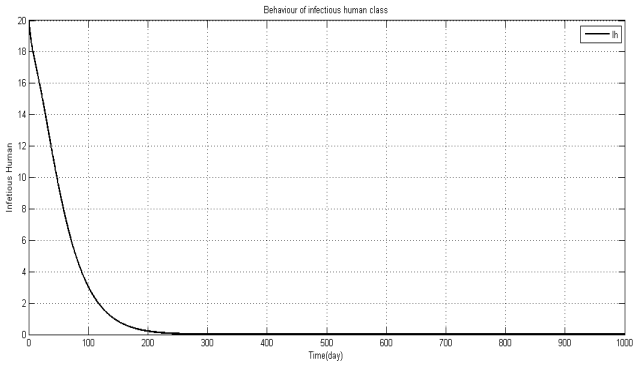

FIGURE 11. Strategy 4, infected human population

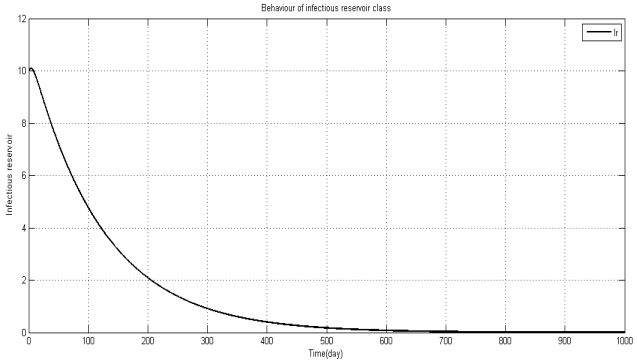

FIGURE 12. Strategy 4, infected reservoir population

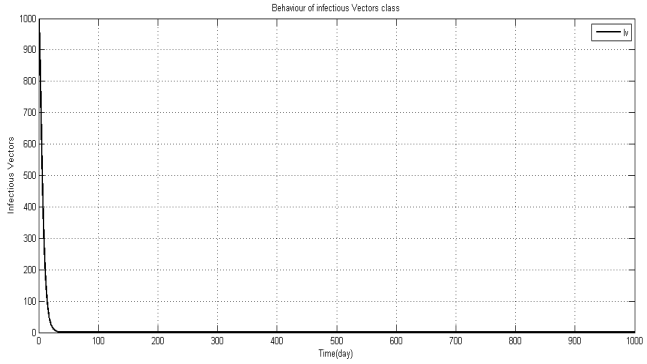

FIGURE 13. Strategy 4, infected vector population

TABLE 4. results of control strategies

$Strategies$	I_hT_s	I_rT_s	I_vT_s
$Strategy1$	285 days	$*$	37 days
$Strategy2$	253 days	$*$	34 days
$Strategy3$	273 days	$*$	34 day
$Strategy4$	256 days	721 days	32 days

$*$ Means that the infection cannot be eliminated in long period.

calculate the sensitivity indices of different parameters involved in R_0 and propose some strategies to control the disease on the basis of the indices of parameters.

All the parameter used in R_0 effect the initial transmission rate of infection at different rates. The control of some parameters reduce infection in human population but on the other hand cause an increase in the level of infection in reservoir population and vice versa. This is infact, a big hurdle in designing a control strategy. We propose control strategies based on biting rate of sand fly, transmission probabilities of disease from sand fly to both reservoirs and humans and vice versa, culling rate of dogs, mortality rate and birth rate of sand flies.

In Strategy (1), we keep the biting rate of sand flies high (un-interrupted) and the culling rate of dogs low. As a result we observe that the infection eliminates from human and sand fly classes. The strategy seems to be fair enough but the drawback of the strategies is that it cannot eliminate the infection from the reservoir class in short time. The same drawbacks can be observed in strategies (2) and(3).

In strategy (4); we reduce the contact rate of sand flies and humans, using bed nets and repulsive chemical lotions. Also we reduce the culling rate of infectious dogs. As a result we have sufficient decrease in all the three infected class of human, sand flies and reservoirs. The strategy confirms the complete eradication of the disease with in the period of about

two years.

The agency fighting against Leishmaniasis can opt any of the four strategies. However we recommend strategy (4), because as a result of this strategy the infection in reservoir class eliminates quickly. Otherwise, the prolonged infectiousness of reservoir class may facilitate reinfection of the disease in the community and hence challenges the global stability of disease free state.

In future work, we intend to analyze the results of the strategies with help of different methods, like variational iteration method and homotopy perturbation method etc.

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